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Survival Mixtrue Model of Gamma Distribution F of Modelling Heterogeneous Data

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Abstract
In this study survival mixture model of three components was proposed for the analysis of heterogeneous survival data. The proposed model constitutes of three components survival mixture model of the Gamma distribution. The properties of model were highlighted. Both simulated and real data were used to estimate the maximum likelihood estimators of the model by employing the Expectation Maximization (EM). Three different censoring percentages (10%, 20% and 40%) were employed in the simulated data to assess the performance of the proposed model with different censoring percentages. The comparison showed that the model performed well with the three censoring percentages. However, the estimated parameters were better with small censoring percentage. The real data were used to compare the proposed model with the pure classical parametric survival models corresponding to each component, the two and four components survival mixture models of the Gamma distributions. The Log-likelihood (LL) and the Akaike Information Criterion (AIC) values showed that the proposed model represents real data better than the pure classical survival model, the two and four components survival mixture models of the Gamma distributions. The proposed model showed that survival mixture models are flexible and maintain the features of the pure classical survival model and are better option for modelling heterogeneous survival data.

Keywords: Simulated data, Real data, Mixture model, Three components, Gamma distribution

INTRODUCTION

Survival analysis investigates particular event happening within a given period of time. Survival analysis methods are applied in different fields such as Medical studies, biology, social sciences, economic and engineering to mention few. The nonparametric methods are commonly employed in analysing survival data. Pure classical parametric survival models are very powerful methods in survival analysis; they are preferred over the nonparametric methods when the chosen distribution seems to fit the data properly. The Gamma distribution is among the most commonly used distributions in the literature for modelling survival data [1], [2], [3] and [4]. When the data are believed to be heterogeneous in nature, survival mixture models are most appropriate for modelling such type of data. In the recent decades, many authors employed the methods of mixture models to analyse survival data. A two components survival mixture model of Weibull distributions was proposed where the parameters of the model were estimated by the weighted least squares method [5]. Two components survival mixture model of Weibull distributions was proposed, where the parameters of the model were estimated by graphical approach [6]. Also a new technique was developed for evaluating the parameters of a two components survival mixture model of Weibull distributions [7].

The Expectation Maximization (EM) was employed to evaluate the parameters of a two-component survival mixture model of the Weibull-Weibull distributions, and the model stability was investigated by employing simulated data [8]. Two components survival mixture models of Gamma-Gamma, Weibul-Weibull and Lognormal-Lognormal distributions were used to model heterogeneous survival data [9]; they implemented model selection technique to select the model which better represents the real data. A survival mixture of mixed distribution was proposed to model heterogeneous data. The model was a two components survival model of the Extended Exponential-Geometric (EEG) distribution [10].

Three components survival mixture models did not receive much attention. A study was conducted to observe the risk of death after open-heart surgery [11]. The study was able to classify the risk of death after the surgery by three different time overlapping phases which are better analysed by a three components survival mixture model, as was pointed out by [12] and [13]. Another study proposed a three components survival mixture model of Weibull distributions to model survival data. The study employed Bayesian method to estimate the parameters of the model [14]. Expectation Maximization Algorithm (EM) was proposed and employed on data believed to consist of some missing or unobserved observations [15]. The parameters of survival mixture models are commonly evaluated by implementing the EM Algorithm [16] and [17].

In this study simulated and real data were used to investigate the flexibility and appropriateness of a three components survival mixture model of the Gamma distribution in modelling heterogeneous survival data. The arrangement of the paper is as follows. In section two the survival analysis and some properties of the Gamma distribution were highlighted. Section three devoted to discussing mixture model of three components in the survival analysis. Section four highlighted the employment of the EM in estimating the maximum likelihood parameters of the proposed model. Section five devoted to data application to evaluate the parameters of the proposed model where both simulated and real data were used. Section six devoted for summary and conclusion.

SURVIVAL ANALYSIS AND THE GAMMA DISTRIBUTION

Survival analysis concern with the application of some statistical method to model and analyse survival data. The focus of interest is the occurrence of a particular event of interest within a given period of time. The response of primary interest *T* is a non-negative random variable which gives the survival time of an object or an individual which can be represented by three important functions. The probability density function (pdf) denoted by $f(t)$, which is written as

$$f(t) = \frac{dF(t)}{dt} \quad (1)$$

Where $F(t)$ is the distribution function of response variable *T*. The probability density function can also be presented graphically, the graph of $f(t)$, is known as the density curve. The density function $f(t)$ is a nonnegative function and the area between the curve and the t axis is equal to 1. The survival function denoted by $S(t)$ can be written as

$$S(t) = 1 - F(x) \quad (2)$$

Which gives the probability that an individual will survive beyond a particular time *t*. Note that the survival function $S(t)$ is a monotonic decreasing continuous function with $S(0) = 1$ and $S(\infty) = 0$. The hazard function can be represented by $h(t)$, and is given by

$$h(t) = \frac{f(t)}{S(t)} \quad (3)$$

which gives the probability of an individual to fail within a small interval $(t, t + \Delta t)$, provided that the individual was a life until the beginning of that interval.

Pure classical parametric survival models are powerful method in survival analysis; when the chosen probability distribution appropriately represents the data. The Gamma probability distribution is among the most important distributions employed in survival data [2], [3] and [4]. The probability density function $f(t)$ and survival functions $S(t)$ of the Gamma distribution are highlighted below.

Gamma distribution

$$f_{Gm}(t) = t^{\alpha-1} e^{-t/\beta} (\beta^{\alpha}\Gamma(\alpha))^{-1} \quad t \text{ and } \alpha, \beta > 0 \quad (4)$$

$$S_{Gm}(t) = 1 - \frac{\Gamma_x(\alpha)}{\Gamma(\alpha)} \quad (5)$$

Where $\Gamma_x(\alpha)$ is known as the incomplete Gamma function.

SURVIVAL MIXTURE MODEL OF THREE COMPONENTS

In survival analysis, mixture models are frequently used because they are flexible. They are the best option where pure classical parametric survival models do not fit the data of Thus heterogeneous nature [16] and [18]. Survival mixture model of three components is used when it is believed that the data consist of three subpopulation or subgroups. Equation 6 represents a parametric survival mixture model of three components.

$$f_{X,Y,Q}(t;\Theta) = \pi_1 f_X(t;\theta_X) + \pi_2 f_Y(t;\theta_Y) + \pi_3 f_Q(t;\theta_Q) \quad (6)$$

Where the vector $\Theta = (\pi_1, \pi_2, \theta_X, \theta_Y, \theta_Q)$, represents the vector the parameters of the mixture model. The functions $f_X(t;\theta_X), f_Y(t;\theta_Y)$ and $f_Q(t;\theta_Q)$ are the probability density functions corresponding to each component with some parameters θ_X, θ_Y and θ_Q respectively.

In this paper a survival mixture model of three components is proposed to model heterogeneous survival data. The survival mixture model of the Gamma distributions is defined as

$$f_{G1\_G2\_G3}(t;\Theta) = \pi_1 f_{G1}(t;\alpha_1,\beta_2) + \pi_2 f_{G2}(t;\alpha_2,\beta_2) + \pi_3 f_{G3}(t;\alpha_3,\beta_3) \quad (7)$$

Where π_i's represent the percentage of the three subpopulations with the sum of $\pi_i's$ equals to 1. The functions f_{G1}, f_{G2} and f_{G3} are the probability density functions of the Gamma distribution corresponding to each component.

EXECTATION MAXIMIZATION ALGORITHM (EM)

One of the most efficient and effective methods commonly employed to estimate the maximum likelihood estimators of finite mixture models is the EM [17].

Let $t_1, t_2, \ldots, t_n$ be a set of observations of *n* incomplete data and z_1, z_2, z_3 be a set of missing observations, where $z_{ki} = z_K(t_i) = 1$, if the observation belongs to the k^{th} component and 0 otherwise for $k = 1,2,3$ and $i = 1,\ldots,n$. On the implementation of the EM to the mixture model, the variables z`s are considered as missing values. The EM consists of two different steps, the first one is the Expectation step or the E-step and the second one is the Maximization step or the M-step.

The z_i variables are treated as missing observations in the E-step, the hidden variable vector $z_i = [z_{1i}, z_{2i}, z_{3i}]$ are estimated by the evaluation of the expectation $E(z_{ki}|t_i)$.

$$\hat{z}_{1i} = E(z_{1i} \mid t_i) = \frac{\pi_1 f_X(t_i;\theta_X)}{\pi_1 f_X(t_i;\theta_X)+\pi_2 f_Y(t_i;\theta_Y)+\pi_3 f_Q(t_i;\theta_Q)} \tag{8}$$

$$\hat{z}_{2i} = E(z_{2i} \mid t_i) = \frac{\pi_2 f_Y(t_i;\theta_Y)}{\pi_1 f_X(t_i;\theta_X)+\pi_2 f_Y(t_i;\theta_Y)+\pi_3 f_Q(t_i;\theta_Q)} \tag{9}$$

$$\hat{z}_{3i} = E(z_{3i} \mid t_i) = \frac{\pi_3 f_Q(t_i;\theta_Q)}{\pi_1 f_X(t_i;\theta_X)+\pi_2 f_Y(t_i;\theta_Y)+\pi_3 f_Q(t_i;\theta_Q)} \tag{10}$$

The functions $E(z_{1i}|t_i)$, $E(z_{2i}|t_i)$ and $E(z_{3i}|t_i)$ calculated in the E-step will be maximized in the M-step of the EM under the condition the sum of $\pi_i's$ equals to 1. The evaluation of the mixing probabilities $\pi_i's$ and vector of parameter $\theta = [\theta_X, \theta_Y, \theta_Q]$, is by the implementation of the Lagrange method. The mixing probabilities will be obtained by;

$$\hat{\pi}_1 = \sum_{i=1}^{n} \hat{z}_{1i} \Big/ n \tag{11}$$

$$\hat{\pi}_2 = \sum_{i=1}^{n} \hat{z}_{2i} \Big/ n \tag{12}$$

$$\hat{\pi}_3 = \sum_{i=1}^{n} \hat{z}_{3i} \Big/ n \tag{13}$$

The maximum likelihood estimators of the parameters α and β of the Gamma distribution for the proposed model are evaluated using equations 14 and 15 respectively.

$$\hat{\alpha}_{(r+1)} = \hat{\alpha}_r - \frac{\ln(\hat{\alpha}_r) - \Psi(\hat{\alpha}_r) - \ln\left(\frac{\sum_{t=1}^{n} \hat{z}_{ji} t_i}{\sum_{t=1}^{n} \hat{z}_{ji}}\right) + \frac{\sum_{t=1}^{n} \hat{z}_{ji} \ln(t_i)}{\sum_{t=1}^{n} \hat{z}_{ji}}}{\frac{1}{\hat{\alpha}_r} - \Psi'(\hat{\alpha}_r)} \tag{14}$$

$$\hat{\beta} = \left(\hat{\alpha} \sum_{i=1}^{n} \hat{z}_{ji}\right)^{-1} \sum_{i=1}^{n} \hat{z}_{ji} t_i \tag{15}$$

Where $j=1,2,3$, r is the number of Newton-Raphson iteration within EM Algorithm and $\Psi(.)$ and $\Psi'(.)$ are a digamma and trigamma functions respectively.

DATA ANALYSIS

Simulated Data

In this section three sets of data of size 200 with 10%, 20% and 40% censoring observations respectively were considered for the validation of the performance of the proposed model using simulated data. The mixing probabilities employed were arranged in descending order (50%, 30% and 20%). Survival data of size 200 observations were generated based on mixture model of three well separated components of Gamma distribution. The parameters of the first component of Gamma distribution (G1) are ($\alpha_1 = 40$, $\beta_1 = 20$), the parameters for the second component of Gamma distribution (G2) are ($\alpha_2 = 6$, $\beta_2 = 1$) and the parameters of the third component of Gamma distribution (G3) are ($\alpha_3 = 200$, $\beta_3 = 20$). These parameters were adopted from a study that employed Bayesian estimation method to analyse the survival mixture model of Gamma distribution [19]. Samples of size 200 were generated from the Exponential distribution for the censored time C with (b), where the value of b depends solely of the percentage of the observations that are censored. In this study 10%, 20% and 40% censoring observations were considered for each of the sample generated in which, $t_j = \min(T_j, C_j)$ was taken as the minimum of the survival time and the censored time of the observed time T where

$$T = \begin{cases} \delta_i = 1, & if \;\; X \le C, \\ \delta_i = 0, & if \;\; X > C. \end{cases} \quad (16)$$

The proposed model was formed by substituting the values of the parameters mentioned earlier. Thus,

$$f(t) = 0.5 * f_{G1}(t; \alpha_1 = 40, \beta_1 = 20) + 03 * f_{G2}(t; \alpha_2 = 6, \beta_2 = 1) + 0.2 * f_{G3}(t; \alpha_3 = 200, \beta_3 = 20) \quad (17)$$

where the density function f_G represents the Gamma distribution probability density functions corresponding to each component of proposed model.

The simulated data were used to estimate the parameters of the proposed model by employing the EM. Table 1 displays the result of the estimates of the parameters of the proposed model for the three different censoring percentages.

Table 1 The Estimated Parameters of the Simulated Data of size 200

Sample size 200 observations and 10% censoring								
Parameter	π_1	π_2	α_1	α_2	α_3	β_1	β_2	β_3
Postulate	0.50	0.30	40	6	200	20	1	20
Estimates	0.49	0.29	40.00	6.00	200.00	20.01	1.00	19.41
Sample size 200 observations and 20% censoring								
Parameter	π_1	π_2	α_1	α_2	α_3	β_1	β_2	β_3
Postulate	0.50	0.30	40	6	200	20	1	20
Estimates	0.47	0.28	40.05	5.69	199.99	20.0	0.91	19.25
Sample size 200 observations and 40% censoring								
Parameter	π_1	π_2	α_1	α_2	α_3	β_1	β_2	β_3
Postulate	0.50	0.30	40	6	200	20	1	20
Estimates	0.41	0.23	40.09	4.80	199.95	20.15	0.74	19.19

The parameters for the three sets of the simulated data were estimated successfully. From Table 1, it can be observed that the estimated parameters are all close to the postulated parameters used in the data generation. Also the parameter for the simulated set of data with 10% censoring are more closer the true parameters compared to that of the 20% and 40% censored observations. The estimation of the mixing probabilities was more accurate in sample with 10% censoring.

The probability density function of the simulated data of the proposed model, with 200 observations and 10%, 20% , 40% censoring percentages respectively, and the probability density functions of pure classical survival model (G1, G2 and G3) corresponding to the components of the proposed model are displayed in Figures 1, 2 and 3.

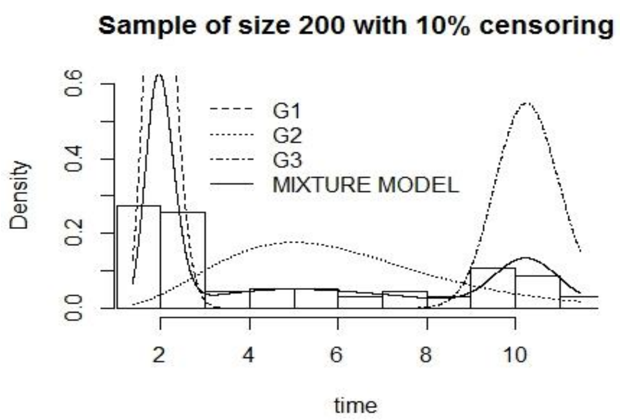

Figure 1: Density of the Simulated Data for the Proposed Model with 10% Censoring

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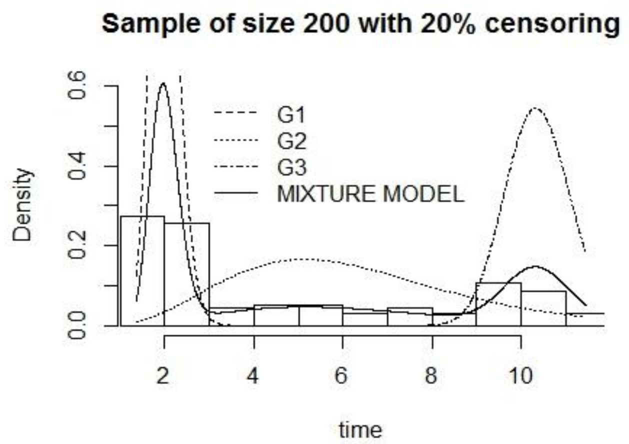

Figure 2: Density of the Simulated Data for the Proposed Model with 20% Censoring

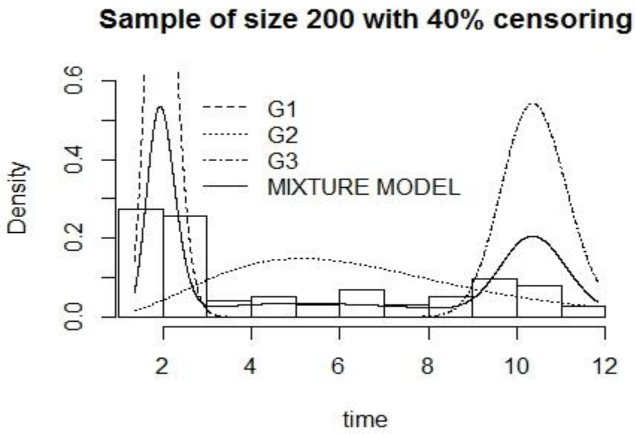

Figure 3: Density of the Simulated Data for the Proposed Model with 40% Censoring

The simulation of the three sets of the generated data of 200 observations with 10%, 20% and 40% censored observations were repeated 300 times to check the consistency and stability of the proposed model. The averages, the mean square errors (MSE) and root mean square error (RMSE) of estimated parameters were listed in Table 2.

Table 2: The Repeated Simulation of Set of 200 Observations

Sample size 200 and 10% censoring								
Parameters	π_1	π_2	α_1	α_2	α_3	β_1	β_2	β_3
Postulates	0.50	0.30	40	6	200	20	1	20
Estimates	0.48	0.29	40.61	5.38	199.28	20.32	0.87	19.65
MSE	5.68e-7	1.63e-6	6.28e-2	1.48e-4	1.70e-1	1.59e-2	5.63e-5	1.90e-3
RMSE	7.53e-4	1.28e-3	2.51e-1	1.21e-2	4.12e-1	1.26e-1	7.51e-3	4.36e-2
Sample size 200 and 20% censoring								
Parameters	π_1	π_2	α_1	α_2	α_3	β_1	β_2	β_3
Postulated	0.50	0.30	40	6	200	20	1	20
Estimates	0.45	0.27	40.50	4.34	196.87	20.25	0.65	18.93
MSE	1.09e-6	1.97e-6	8.30e-2	1.64e-3	5.08e-1	2.07e-2	6.57e-5	5.03e-3
RMSE	1.04e-3	1.40e-3	2.87e-1	4.05e-2	7.13e-1	1.44e-1	8.11e-3	7.09e-2
Sample size 200 and 40% censoring								
Parameters	π_1	π_2	α_1	α_2	α_3	β_1	β_2	β_3
Postulated	0.50	0.30	40	6	200	20	1	20
Estimates	0.41	0.26	41.13	3.68	195.98	20.56	0.52	18.40
MSE	1.55e-6	2.45e-6	7.81e-2	1.61e-3	6.71e-1	1.98e-2	5.72e-5	6.36e-3
RMSE	1.24e-3	1.57e-3	2.80e-1	3.75e-2	8.19e-1	1.41e-1	7.57e-3	7.97e-2

The averages of the parameters are close to the parameters of the postulated with MSE and RMSE relatively small, which suggests that, the EM performed consistently in estimating the parameters. The MSE corresponding to the mixing probabilities are relatively smaller for the 10% censoring as compared to the 20% and 40% censoring. Also the MSE for the parameters of the components are smaller for the 10% censoring compared to that of the 40%. Generally, the estimation of the mixing probabilities and the parameters are seemed to be closer to the true value with smaller censoring percentage 10% than with 20% and 40%.

Real Data

The real data analysed in this section is the Kidney Catheter data. The data are included as one of the data set in the famous *survival* package developed by [20] of the R statistical software [21]. The data give the recurrence times to infection, at the point of insertion of catheters for kidney patients using portable dialysis equipment. The probability density function of proposed model and the pure classical survival models of the Gamma distribution corresponding to each of the components were plotted together with the histogram of the Kidney Catheter data in Figure 4. The graph indicates that the proposed model fits the data better than the individual pure classical survival models of the Gamma distributions corresponding to each component.

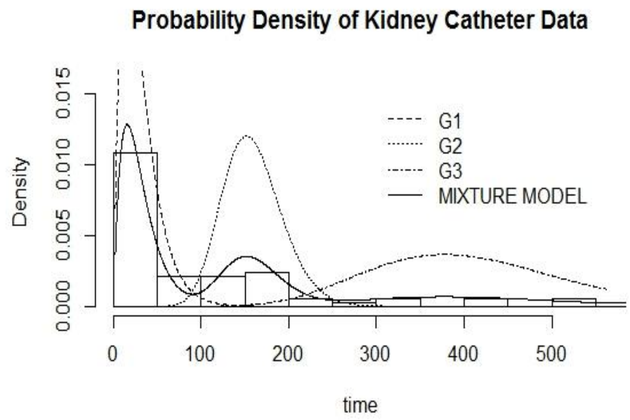

Figure 4: Density Function of Proposed Model Using Kidney Catheter Data

Table 3 displays estimated parameters of proposed model using the Kidney Catheter data. The mixing probabilities were in descending order.

Table 3: The Estimated Parameters of the Proposed Model of Kidney Catheter Data

Parameter	π_1	π_2	α_1	α_2	α_3	β_1	β_2	β_3
Estimates	0.53	0.29	2.06	21.97	13.05	14.75	7.14	31.28

The parameters, LL, AIC, MSE, RMSE and Kolmogorov-Smirnov K-S test values were estimated and reported. Table 4 shows that proposed model scored higher value for the LL (-331.57) than the values (-341.20) scored by the pure classical survival parametric model of the Gamma distribution. Also, the AIC value (679.13) of the model was smaller compared to corresponding value (686.40) of the pure classical parametric survival model of the Gamma distribution. The MSE of the fitted model (0.0108) is smaller than that of the pure classical model (0.0194). This result indicates that the Kidney Catheter data seem to be appropriately fitted by the proposed model.

Table 4: Estimated Parameters of the Proposed Model for Kidney Catheter Data

Model	Estimates	LL	AIC	MSE	RMSE	K-S
Pure classical	$\hat{\alpha}$ = 0.89, $\hat{\beta}$ = 156.96	-341.20	686.40	0.0194	0.1392	0.25 (0.02)
Proposed model	$\hat{\alpha}_1$=2.06, $\hat{\beta}_1$= 14.75 $\hat{\alpha}_2$ = 21.97, $\hat{\beta}_2$= 7.14 $\hat{\alpha}_3$ = 13.05, $\hat{\beta}_3$= 31.28 $\hat{\pi}_1$ = 0.53, $\hat{\pi}_2$= 0.29	**-331.57**	**679.13**	**0.0108**	**0.1038**	**0.16 (0.30)**

The K-S test statistic of proposed model (0.16) with the p-value in bracket shows that the model fits the data better than the pure classical survival distribution.

The survival function graph was compared with the K-M empirical survival function of the real data to investigate the fit of proposed model. The survival function of the model and the K-M empirical survival function were presented in Figure 5.

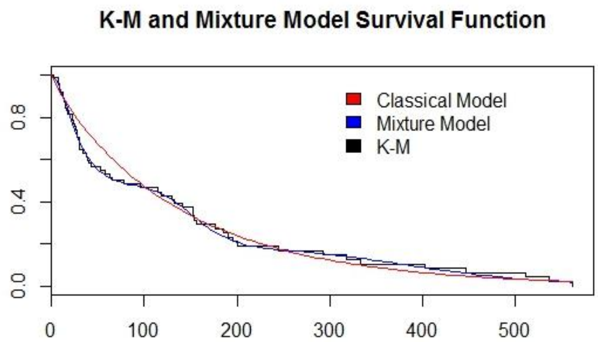

Figure 5: K-M, Survival Function of Proposed Model and the Pure Survival Model

In Figure 5 the K-M empirical survival function is in solid black, the survival function of proposed model is in dark blue, the pure classical survival model of the Gamma distribution is in red. Form the Figure it can be observed that the survival function of the proposed model is in full agreement with the K-M empirical survival function much better than the pure classical survival model.

The histogram of the Kidney Catheter data shows that mixture structure is appropriate for the data; hence the AIC model selection was used to determine the sub-population that fits the data.

Model selection was performed among the proposed model, the two and the four components parametric survival mixture models of the Gamma distributions to select the model that represents Kidney Catheter data better by applying the LL and AIC criterion. Table 5 gives the LL and the AIC corresponding to each parametric survival mixture model of the Gamma distributions. The LL value of Model 1 (-331.57) is higher than that of the two, four components parametric survival mixture model of the Gamma distributions (-334.90), (-336.88) respectively. The AIC criterion value of proposed model (679.13) is smaller than that of the two and four components parametric survival mixture model of the Gamma distributions respectively.

Table 5: The LL and AIC Values of the Parametric Survival Mixture Models of the Gamma Distribution

Number of components		**2 (G1_G2)**	**3 (Proposed Model)**	**4 (G1_G2_G3_G4)**
Mixture of Gamma	LL	-334.90	-331.57	-336.88
	AIC	681.80	679.13	695.76

The result shows that both the LL and AIC are in support of proposed model. Three sub-populations fit the Kidney Catheter data much better than the two, four sub-populations survival mixture model and the pure classical survival model.

CONCLUSIONS

The paper proposed a three components survival mixture model of the Gamma distribution to model heterogeneous survival data. Simulated and real data were used to evaluate the model. EM algorithm was employed in estimating the maximum likelihood estimator of the parameters. The simulated data used to compare the effect of different censoring percentages revealed that the model performed much better with small percentage of censored observations. The comparison of the proposed model with the pure classical parametric survival model and the survival mixture models of two and four components of Gamma distribution revealed that the real data were better represented by the proposed model. The proposed model showed that the survival mixture models are flexible and maintain the feature of pure classical parametric survival models and they are better options to model heterogeneous survival data.

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